Dietary medium-chain triacylglycerol prevents the postprandial rise of plasma triacylglycerols but induces hypercholesterolemia in primary hypertriglyceridemic subjects[1–3]

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ABSTRACT

Background: Previous studies showed divergent results concerning the influence of medium-chain triacylglycerol (MCT) on lipoprotein metabolism.

Objective: The objective of this study was to compare the effects of MCT and corn oil on plasma lipids in primary hypertriglyceridemic patients.

Design: Ten subjects ate different proportions of corn oil and MCT for 12 wk. The subjects first ate a low-fat diet for 2 wk and during the next 4 wk, corn oil was added as the sole source of fat. Thereafter, for 2-wk periods, the subjects were sequentially fed corn oil and MCT mixed in the following proportions: 3:1, 1:1, and 0:1. Fasting plasma total cholesterol, triacylglycerol, and HDL-cholesterol concentrations were measured at the end of each period. At the end of the 100%–corn oil and of the 100%-MCT periods, subjects were fed a test meal containing the respective oil (40 g fat/m^2 body surface area) and total cholesterol and triacylglycerols were measured at 2-h intervals over 8 h; fasting lipoprotein composition was also measured.

Results: Compared with corn oil, MCT was associated with a higher mean (±SD) fasting total cholesterol concentration (6.39 ± 1.14 compared with 5.51 ± 0.98 mmol/L, respectively; $P < 0.05$); non-HDL-cholesterol concentrations were also higher with MCT (5.36 ± 1.11 mmol/L) than with corn oil (4.51 ± 0.92 mmol/L; $P < 0.005$). In response to the liquid test meal, plasma total cholesterol did not change with either diet but triacylglycerols increased with the 100%–corn oil diet.

Conclusions: MCT prevents the risk of pancreatitis due to postprandial hypertriglyceridemia but has the inconvenience of raising total cholesterol concentrations in primary hypertriglyceridemic subjects. *Am J Clin Nutr* 2000;71:701–5.

KEY WORDS Medium-chain triacylglycerol, corn oil, hypertriglyceridemia, hypercholesterolemia, lipoprotein metabolism, test meal, nonobese adults

INTRODUCTION

Medium-chain triacylglycerol (MCT) has been used for ≈50 y in the treatment of disorders of lipid absorption due to pancreatic lipase deficiency and as a source of energy in enteral and parenteral nutrition (1). MCT contains mainly 8–10-carbon fatty acids that facilitate the action of the pancreatic lipase, and large amounts of MCT are absorbed as triacylglycerols in patients deficient in pancreatic lipase (1). Hydrolysis of MCT to its component fatty acids is faster and more efficient than that of long-chain triacylglycerol (LCT), and the medium-chain fatty acids (MCFAs) bound to albumin reach the liver by the portal system without being incorporated into chylomicrons (1, 2). However, other studies showed that, in the liver, MCFAs may be reesterified to triacylglycerols after elongation of the carbon chain (3, 4) instead of being completely oxidized to ketone bodies (1, 2, 5).

In contrast, LCT must be hydrolyzed by pancreatic lipase and, after intestinal absorption, long-chain fatty acids (LCFAs) are reesterified to triacylglycerols, packaged as chylomicrons, and transported out of the cells into the lymphatic system (6). Several studies were conducted on the influence of MCT on serum lipid and lipoprotein metabolism, but some results are divergent. One study in healthy subjects showed that, compared with LCT, MCT produces significantly higher plasma concentrations of triacylglycerols without modifying total cholesterol (7) but that the opposite occurs when MCT is compared with myristic and oleic acids (8). MCT also resulted in a significantly greater frequency of cholesterolemia in mildly hypercholesterolemic men than did a high oleic acid sunflower oil feeding (9).

In healthy subjects, plasma total cholesterol concentrations with an MCT-supplemented diet were higher than with a corn oil–supplemented diet but lower than with a butter-enriched diet (10). Compared with safflower and coconut oils, MCT produced

[1] From the Lipids Laboratory (LIM 10), University of São Paulo Medical School, São Paulo, Brazil.

[2] Corn oil provided by Refinações de Milho Brasil Ltda, São Paulo, Brazil; medium-chain triacylglycerol provided by Nutricia Produtos Dietéticos e Nutricionais SA, São Paulo, Brazil; skim milk provided by Nestlé Indústria e Comércio Ltda, São Paulo, Brazil; and lyophilized mixture provided by Liotécnica Indústria e Comércio Ltda, Laboratórios de Investigação Médica (LIM), Hospital das Clínicas, São Paulo, Brazil.

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TABLE 1
Fatty acid composition of oils added to the diet[1]

Fatty acid	Corn oil	Medium-chain triacylglycerol
	% by wt	
8:0	Traces	72
10:0	Traces	24
14:0	Traces	Traces
16:0	12.4	Traces
18:0	2.2	Traces
18:1	33.5	Traces
18:2	49.0	Traces
18:3	1.1	Traces

[1] Data from Refinações de Milho Brasil Ltda, São Paulo, Brazil, and Unichema International, Barcelona, Spain.

higher triacylglycerol concentrations in patients with diabetes and in obese patients (11) and in overfed, healthy, nonobese males (12). Several reviews were published on the physiology of MCT and on its clinical nutritional use (1, 2, 5, 13), but, except for in patients with lipoprotein lipase deficiency (14, 15), no studies are available on hypertriglyceridemic subjects in general, although they are likely to also benefit from MCT in the diet. The objective of the present investigation in primary hypertriglyceridemic patients was to compare the effects on fasting and postprandial plasma lipids and lipoproteins of a stepwise rise in the proportion of MCT in the diet.

SUBJECTS AND METHODS

Subjects

Ten nonobese, adult outpatients (6 women and 4 men) with plasma triacylglycerol concentrations between 2.82 mmol/L (250 mg/dL) and 11.29 mmol/L (1000 mg/dL) were recruited at the Hospital of the University of São Paulo Medical School and enrolled in a dietary protocol. None of the subjects had diabetes, renal or hepatic diseases, or other secondary causes of hyperlipidemia or had been taking medications that interfere with lipid metabolism for ≥2 mo before admission to the study. The subjects were aged between 34 and 68 y. All subjects gave their written, informed consent to participation in the study, which was approved by the Ethical Committee of the Hospital of the University of São Paulo Medical School.

Dietary protocol

All subjects consumed ad libitum their daily diet with added corn oil (Refinações de Milho Brasil Ltda, SP, São Paulo, Brazil), MCT (Unichema International, Barcelona, Spain), or both. The oils were given to the patients once a week in 500-mL bottles and the amounts not consumed were measured. The fatty acid composition of each oil as stated by the suppliers is shown in **Table 1**. The 12-wk study protocol included 5 study periods. All subjects first consumed a low-fat diet in which intrinsic fat accounted for 10.5 ± 4.6% ($\bar{x}$ ± SD) of total energy intake for 2 wk. Thereafter they received additional corn oil as the sole visible source of fat in their diet for 4 wk. In the ensuing 3 periods, each lasting 2 wk, all subjects were sequentially given mixtures of oil with the following ratios of corn oil to MCT: 3:1, 1:1, and 0:1. Throughout the study, all subjects were instructed to avoid alcoholic beverages, to consume very-low-fat foods, and to eat the added oil ad libitum.

All subjects were regularly asked about their dietary habits and fat tolerance, and a 24-h food record was obtained once during the period in which the oils were consumed in a 1:1 ratio for the purpose of evaluating the subjects' total energy intake and energy intake from fat. At the end of the 100%–corn oil and of the 100%-MCT periods, the subjects consumed a test meal that provided 40 g fat/m^2 body surface area; this meal consisted of a lyophilized mixture (percentage by weight) containing 20% protein (lactoalbumin, from skim milk; Nestlé Industry, São Paulo, Brazil), 55% carbohydrate (sucrose), and 25% of the oil (corn oil or MCT) that had been eaten during the respective period. The purpose of the test meal was to measure postprandial lipid variation after an acute fat load. The mixture was prepared by adding hot water and was consumed over a 10-min period. During the test meals the subjects were allowed water ad libitum.

Lipid and lipoprotein analyses

On the first day of the initial diet period, fasting blood samples were collected in EDTA-coated tubes for lipid analyses. Thereafter, blood samples were drawn twice in the low-fat, 100%–corn oil, and 100%-MCT diet periods and once in the periods during which 75% corn oil plus 25% MCT and 50% corn oil plus 50% MCT were fed, and fresh samples and samples stored at –70 °C were analyzed. Plasma total cholesterol and triacylglycerol concentrations were measured by enzymatic assays with commercially available kits (Boehringer Mannheim, Darmstadt, Germany, and Merck KgaA, Buenos Aires, respectively) using Cobas Mira software (version 8847; F Hoffmann-La Roche, Basel, Switzerland). HDL cholesterol was measured after precipitation of apolipoprotein B–containing lipoproteins with magnesium chloride and dextran sulfate (16) and non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol.

Before each test meal, blood samples were drawn on ice into tubes containing 10% EDTA (10 mL/L blood). Plasma was immediately obtained by centrifugation at 1000 × *g* for 10 min at 4 °C in a refrigerated centrifuge (RT 6000B; Sorvall, Newton, CT) and the following preservatives were added per L: 2 mmol benzamidine/L (5 mL), 0.5% gentamycin and 0.25% chloramphenicol (20 mL), 0.87 g phenyl-methyl-sulfonyl-fluoride/L DMSO (0.5 mL), and 10 g aprotinin/L (5 mL). Plasma was then separated by discontinuous gradient density ultracentrifugation (286 000 × *g* for 24 h at 4 °C; L7–55 ultracentrifuge; Beckman, Palo Alto, CA) into fractions at the following densities (g/L): 1006 to obtain VLDL cholesterol, 1020 for intermediate-density (IDL) cholesterol, 1065 for LDL cholesterol, and 1210 for total HDL cholesterol. Lipoprotein fractions were then frozen at −70 °C for further measurements of their contents of total cholesterol, triacylglycerols, total protein, and phospholipid; HDL apolipoprotein A-I content was measured by the immunoturbidimetric method using a commercial kit (Unimate 3 APOA; F Hoffmann-La Roche). Blood samples were drawn after the liquid test meal at 2-h intervals over 8 h for measurements of total cholesterol and triacylglycerol concentrations.

Statistical analyses

Fasting and postprandial cholesterolemia and triglyceridemia, patients' weights, and amounts of oils consumed were analyzed with the Friedman test and Dunn's multiple comparison test as a posttest to compare all pairs if $P < 0.05$. Analyses were

TABLE 2
Body weights of subjects and results of plasma analyses at the end of each diet period[1]

	Low-fat diet	100% corn oil	75% corn oil, 25% MCT	50% corn oil, 50% MCT	100% MCT
Body weight (kg)	64 ± 13	66 ± 14	66 ± 13	65 ± 13	66 ± 13
Oil (g/d)	—	17 ± 8	16 ± 6	19 ± 8	24 ± 14
Total cholesterol (mmol/L)[2]	6.09 ± 0.66	5.51 ± 0.98	5.99 ± 1.27	5.86 ± 1.31	6.39 ± 1.14[3]
Triacylglycerol (mmol/L)[4]	6.36 ± 3.48	5.29 ± 2.86	5.14 ± 3.13	5.16 ± 2.38	6.22 ± 3.19
HDL cholesterol (mmol/L)	0.93 ± 0.12	0.99 ± 1.13	0.87 ± 0.08	0.90 ± 0.11	0.92 ± 0.05
	[7][5]	[10]	[6]	[8]	[9]
Non-HDL cholesterol (mmol/L)[6]	4.97 ± 0.57	4.51 ± 0.92	4.59 ± 1.36	4.55 ± 1.02	5.36 ± 1.11[7]
	[7]	[10]	[6]	[8]	[9]

[1] $\bar{x}$ ± SD; n = 10. MCT, medium-chain triacylglycerol.
[2] To convert to mg/dL, divide by 0.02586.
[3] Significantly different from 100% corn oil, $P < 0.05$ (Friedman test, with Dunn's multiple comparison test as a posttest).
[4] To convert to mg/dL, divide by 0.01129.
[5] n in brackets.
[6] Non-HDL cholesterol = total cholesterol minus HDL cholesterol.
[7] Significantly different from 100% corn oil, $P < 0.005$ (Wilcoxon signed-rank test).

performed with GRAPHPAD, version 2.01, for WINDOWS (Graphpad, San Diego, CA). Non-HDL-cholesterol concentrations with the 100%–corn oil and 100%-MCT diets were analyzed with the Wilcoxon signed-rank test. Differences were considered significant at $P < 0.05$. Postprandial cholesterolemia and triglyceridemia were quantified along time as area under the concentration-versus-time curve above a line drawn through the fasting plasma concentrations.

RESULTS

Clinical characteristics of the subjects (6 women and 4 men aged 49 ± 12 y) and plasma analyses are shown in **Table 2**. The subjects' body weight did not change significantly throughout the study period. In the low-fat-diet period, intrinsic fat accounted for 10.7 ± 4.6% of total energy intake. The 24-h food record showed that total fat (intrinsic plus added) accounted for 21.7 ± 6.3% of total energy intake and that added oil alone accounted for 64% of energy from fat. Added dietary oils were well tolerated and the amounts consumed did not significantly differ during the study. Fasting HDL-cholesterol and triacylglycerol concentrations did not vary significantly during the low-fat and modified-fat diet periods; thus, fasting triglyceridemia was not significantly modified by the increase in the percentage of MCT. When the subjects consumed the test meal at the end of either the 100%–corn oil or the 100%-MCT diet period, fasting total cholesterol was significantly higher (16%) with the 100%-MCT diet than with the 100%–corn oil diet and remained significantly higher during the fat absorption phase, although fat absorption by itself did not influence the concentration of plasma total cholesterol (**Figure 1**). Also, no changes occurred in the other diet periods when the ratio of corn oil to MCT varied. Fasting plasma triacylglycerol concentrations were not significantly different between the MCT and corn oil diets; however, as shown in **Figure 2,** during the fat absorption phase, plasma triacylglycerol concentrations increased with the corn oil but not with the MCT test meal.

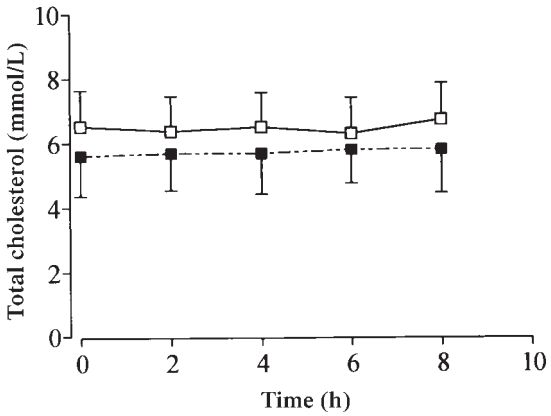

FIGURE 1. Mean (±SD) plasma concentration of total cholesterol after consumption of liquid meals that provided 40 g fat/m^2 body surface area. The fat in the test meals consisted of either corn oil (■) or medium-chain triacylglycerol (□). Areas under concentration-versus-time curve: corn oil, 1.81 ± 0.75 mmol · h/L; MCT, 1.42 ± 1.01 mmol · h/L, Wilcoxon signed-rank test, NS).

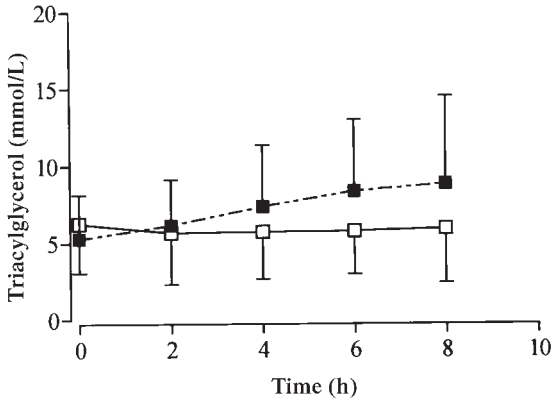

FIGURE 2. Mean (±SD) plasma concentration of triacylglycerol after consumption of liquid meals that provided 40 g fat/m^2 body surface area. The fat in the test meals consisted of either corn oil (■) or medium-chain triacylglycerol (□). Areas under the concentration-versus-time curve: corn oil, 17.94 ± 9.64 mmol · h/L; MCT, 5.02 ± 0.87 mmol · h/L. Significant difference between MCT and corn oil for entire study period, $P < 0.005$ (Wilcoxon signed-rank test).

TABLE 3
Results of plasma analyses at the end of the 100%–corn oil period and at the end of the 100%–medium-chain triacylglycerol (MCT) period[1]

	Total cholesterol	Triacylglycerol	Protein	Phospholipid
		mg/L		
VLDL				
Corn oil	480 ± 270	2680 ± 1310	450 ± 280	1000 ± 470
MCT	610 ± 210	2970 ± 1150	440 ± 210	1050 ± 350
IDL				
Corn oil	190 ± 40	170 ± 70	120 ± 40	250 ± 50
MCT	230 ± 90	370 ± 490[2]	170 ± 110	370 ± 250
LDL				
Corn oil	920 ± 330	290 ± 80	1160 ± 530	870 ± 270
MCT	1030 ± 380	350 ± 90[3]	1130 ± 400	780 ± 290
HDL				
Corn oil	380 ± 70	360 ± 200	1420 ± 320[4]	1060 ± 290
MCT	340 ± 70[3]	310 ± 150	1320 ± 260[4]	1100 ± 380
VLDL + IDL + LDL cholesterol				
Corn oil	1590 ± 410	—	—	—
MCT	1870 ± 250[3]	—	—	—

[1] $\bar{x}$ ± SD; n = 10. IDL, intermediate-density lipoprotein.
[2,3] Significantly different from 100% corn oil (Wilcoxon signed-rank test): [2] $P < 0.005$, [3] $P < 0.05$.
[4] Apolipoprotein A-I content.

Lipoprotein composition analysis (**Table 3**) showed that, during the fasting state, the 100%-MCT diet produced a lower fraction of HDL cholesterol but higher fractions of the other lipoproteins (VLDL, IDL, and LDL cholesterol) than did the 100%–corn oil diet, a result that agrees with the data obtained in whole plasma. The 100%-MCT diet also produced higher triacylglycerol concentrations in IDL- and LDL-cholesterol fractions than did the 100%–corn oil diet.

DISCUSSION

Some studies showed variations in plasma lipids and lipoproteins when MCT was fed to normolipidemic (7, 8) and mildly hypercholesterolemic (9) subjects. However, there are no data on the effects of MCT in hypertriglyceridemic patients, except for the beneficial effects of MCT on the severe hypertriglyceridemia of lipoprotein-lipase-deficient patients. Our study was designed to alter the ratio of corn oil to MCT in the diet gradually because abrupt changes in the types and amounts of fat eaten transiently alter plasma lipid and lipoprotein concentrations (7, 9, 10, 17). All subjects maintained their body weights throughout the investigation. Although the oils were eaten ad libitum, their intake was not significantly modified during any dietary period and accounted for 12.5 ± 1.7% of total energy intake. MCT had the undesirable effect of increasing plasma fasting total cholesterol and non-HDL-cholesterol concentrations, as shown by both the lipoprotein precipitation method and discontinuous gradient density ultracentrifugation. Although the mechanism by which MCT raised plasma total cholesterol is not known, it is likely that the higher proportion of saturated fatty acids in MCT (Table 1) might play a role, together MCFAs, which may undergo elongation in the liver (3, 4) and thus increase the rate of VLDL-cholesterol production.

Fasting plasma triacylglycerol concentrations were not significantly altered by consumption of MCT or corn oil. As expected, postprandial total cholesterol was not influenced by the acute fat load of each test meal. However, postprandial triacylglycerol concentrations, which indicate the extent of the increase in plasma triacylglycerols above fasting values after the meal, were significantly lower with MCT than with corn oil, which might be attributable either to less chylomicron and VLDL-cholesterol formation or to the enhancement of the triacylglycerol-rich lipoprotein clearance rate in hypertriglyceridemic subjects (18, 19). Thus, MCT is useful because it potentially prevents the risk of pancreatitis due to postprandial hypertriglyceridemia; however, in the long run, an MCT-associated increase in atherogenic non-HDL-cholesterol concentrations is a major inconvenience.

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